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Original Research Article

A Hospital Based Retrospective Assessment of Emergency Presentation and Immediate Outcome of Children with Autoimmune Hemolytic Anemia

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Abstract

Aim: This study aims to analyze the clinical spectrum, severity of anemia, challenges in arranging cross matched blood in the emergency department (ED), and treatment outcomes of children with autoimmune hemolytic anemia (AIHA).

Material & Methods: This was a retrospective analysis of data from our digital medical records database. Children, less than 18 years of age diagnosed with AIHA, admitted to the Department of Paediatrics, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India, in between one year were enrolled in the study. Our study included 30 children aged 1 month–18 years.

Results: Females constituted 60% of the study population. The most common clinical feature at diagnosis was fever (70%) followed by pallor (53.34%), fatigue (23.33%), jaundice and skin rash (20% each), bleeding manifestations in 16.66%, and joint pain in 6.66% of children. Positive DAT was 4+ in three children, 3+ in eight children, 2+ positive in seven children, and 1+ positive in 12 children. Mild, severe, and very severe anaemia were observed in 20.7%, 66.66%, and 13.34%, respectively. About 40% (n=12) of cases required intensive care treatment. The reasons for transfer to the intensive care unit were cardiorespiratory failure (10%), severe anemia with congestive cardiac failure (10%), diphtheritic myocarditis with acute kidney injury (3.4%), fulminant hepatic failure (3.34%), severe thrombocytopenia with intracranial hemorrhage (3.34%), respiratory distress (3.34%), and very severe pneumonia (6.66%). AIHA was classified as primary (idiopathic) in 6 cases (20%). AIHA was secondary in 24 cases (80%) such as infection triggered (n=8), systemic lupus erythematosis (n=5), connective tissue disorder (n=4), Evans syndrome (n=3), Wilson disease (n=1), acute leukemia (n=1), neonatal diabetes (n=1), and pure red cell aplasia (n=1).

Conclusion: Identifying secondary causes of pediatric AIHA are essential and larger data from multiple centers will contribute toward creating the best clinical approach and emergency management of children with AIHA.

Keywords: Anemia, Cross-matching, Hemolysis, Pediatric, Transfusion.

Introduction

Emergency presentation of autoimmune hemolytic anemia (AIHA) can be life-threatening as it rapidly worsens and needs to be identified early and treatment initiated immediately Autoimmune Hemolytic Anemia (AIHA) is characterized by the production of autoantibodies directed against erythrocyte antigens leading to premature red cell destruction resulting in their destruction by mononuclear phagocytic or complement system.[1,2] Autoimmune hemolytic anemia (AIHA) is a decompensated acquired hemolysis caused by the host's immune system acting against its own red cell antigens. The disease AIHA is a rare and heterogeneous and the overall incidence in adult is 1 in 80,000 to 1, 00,000 of a given population per year.[3] A rare disease in children, presenting with variable severity. It is estimated that the annual incidence of AIHA in children is around 3 per million under 18 years old. [4] AIHA observed in pediatrics is usually self-limiting and often precipitated by viral infections. On the basis of etiology, AIHA can be primary (37%; no underlying predisposition) or secondary (63%; due to autoimmune diseases, drugs, infections or underlying primary immune deficiencies).[5] AIHA based on type and thermal properties (serological) of the auto-antibody attached to red cells can be warm reactive, paroxysmal cold hemoglobinuria, and cold agglutinin disease.[3] Autoimmune hemolytic anemia is the main cause of acquired extra corpuscular hemolysis in children. It can be primary (or idiopathic) and secondary AIHA presenting with thrombocytopenia (Evans syndrome) which tends to have more chronic and relapsing clinical course. It is important that AIHA is considered in all children with acute onset of anemia ideally before transfusion of blood products. The diagnosis and management of children with AIHA presenting as an emergency involves many challenges related to laboratory methods, selection of blood products, and underlying primary disease.[6]

Thus the aim of the study was to analyze the clinical spectrum, the severity of anemia, challenges in arranging cross-matched blood in the ED, and treatment outcomes of children with AIHA.

Material & Methods

This was a retrospective analysis of data from our digital medical records database. Children, less than 18 years of age diagnosed with AIHA, admitted to the Department Of Paediatrics, Rajendra Institute Of Medical Sciences, Ranchi, Jharkhand, India, in between one year were enrolled in the study. Our study included 30 children aged 1 month–18 years.

Inclusion criteria

- All direct antiglobulin test (DAT)-positive children.
- Exclusion criteria
- All DAT negative were excluded from the study.

The demographic details, presenting complaints, and laboratory parameters of all children were analyzed. Hemoglobin (Hb) level of <9 mg/dl was categorized as mild anemia, Hb between 3 and 6 g/dl was categorized as moderate anemia, and Hb <3 was categorized as very severe anemia [3]. AIHA was diagnosed based on the clinical presentation, a positive DAT. Polyspecific DAT test was performed routinely for all children with clinically suspected AIHA. The severity of AIHA based on DAT positivity was noted. Details of previous transfusion, difficulties related to cross-matching, the requirement

of steroids, and intensive care management were documented. Details of treatment, duration of hospital stay, final diagnosis, and mortality were captured. The outcome was categorized as survivors or non-survivors. Simple descriptive statistics were used in this observational study.

Results

Table 1: Demographic details

Gender	N%
Male	12 (40)
Female	18 (60)
Clinical Features	
Fever	21 (70)
Pallor	16 (53.34)
Fatigue	7 (23.33)
Jaundice	6 (20)
Skin Rash	6 (20)
Bleeding Manifestations	5 (16.66)
Joint Pain	2 (6.66)
Positive DAT	
4+	3
3+	8
2+	7
1+	12
Anaemia	
Mild	6 (20)
Severe	20 (66.66)
Very Severe	4 (13.34)

Females constituted 60% of the study population. The most common clinical feature at diagnosis was fever (70%) followed by pallor (53.34%), fatigue (23.33%), jaundice and skin rash (20% each), bleeding manifestations in 16.66%, and joint pain in 6.66% of children. Positive DAT was 4+ in three children, 3+ in eight children, 2+ positive in seven children, and 1+ positive in 12 children. Mild, severe, and very severe anaemia were observed in 20.7%, 66.66%, and 13.34%, respectively.

Table 2: Reasons for transferring cases to PICU

Reasons for transferring cases to PICU	N%
Cardiorespiratory failure	3 (10)
Severe anemia with congestive cardiac failure	3 (10)
Diphtheritic myocarditis with acute kidney injury	1 (3.34)
Fulminant hepatic failure	1 (3.34)
Severe thrombocytopenia with intracranial hemorrhage	1 (3.34)
Respiratory distress	1 (3.34)
Very severe pneumonia	2 (6.66)

About 40% (n=12) of cases required intensive care treatment. The reasons for transfer to the intensive care unit were cardiorespiratory failure (10%), severe

anemia with congestive cardiac failure (10%), diphtheritic myocarditis with acute kidney injury (3.4%), fulminant hepatic failure (3.34%), severe thrombocytopenia with intracranial hemorrhage (3.34%), respiratory distress (3.34%), and very severe pneumonia (6.66%).

Table 3: Secondary causes of AIHA and the number of cases

Secondary causes of AIHA	N%
Infection triggered	8 (26.66)
Systemic lupus erythematosis	5 (16.66)
Connective tissue disorder	4 (13.34)
Evans syndrome	3 (10)
Wilson disease	1 (3.34)
Acute leukemia	1 (3.34)
Neonatal diabetes	1 (3.34)
Pure red cell aplasia	1 (3.34)

AIHA was classified as primary (idiopathic) in 6 cases (20%). AIHA was secondary in 24 cases (80%) such as infection triggered (n=8), systemic lupus erythematosis (n=5), connective tissue disorder (n=4), Evans syndrome (n=3), Wilson disease (n=1), acute leukemia (n=1), neonatal diabetes (n=1), and pure red cell aplasia (n=1).

Discussion

Emergency presentation of autoimmune hemolytic anemia (AIHA) can be life-threatening as it rapidly worsens and needs to be identified early and treatment initiated immediately. AIHA is a rare and heterogeneous disease that affects 1–3/100,000 patients per year.[7] Autoimmune hemolytic anemia is the main cause of acquired extra corpuscular hemolysis in children. AIHA can be primary (or idiopathic) and secondary AIHA presenting with thrombocytopenia (Evans syndrome) which tends to have more chronic and relapsing clinical course. It is important that AIHA is considered in all children with acute onset of anemia ideally before transfusion of blood products. The diagnosis and management of children with AIHA presenting as an emergency involves many challenges related to laboratory methods, selection of blood products, and underlying primary disease.[8]

Females constituted 60% of the study population. The most common clinical feature at diagnosis was fever (70%) followed by pallor (53.34%), fatigue (23.33%), jaundice and skin rash (20% each), bleeding manifestations in 16.66%, and joint pain in 6.66% of children. Positive DAT was 4+ in three children, 3+ in eight children, 2+ positive in seven children, and 1+ positive in 12 children. Mild, severe, and very severe anaemia were observed in 20.7%, 66.66%, and 13.34%, respectively. Fever as a presenting symptom, associated with pallor and jaundice, a common finding in our study, has been described in primary AIHA in children.[9] Data by Fan et al. showed that primary AIHA accounted for 39.7% and secondary AIHA accounted for 60.3%.[10] The availability of newer diagnostic tests could be a reason for secondary AIHA being more common (86%) in our cohort and the majority were infection associated. French National observational study has identified secondary AIHA in 63% of cases.[11]

About 40% (n=12) of cases required intensive care treatment. The reasons for transfer to the intensive care unit were cardiorespiratory failure (10%), severe anemia with congestive cardiac failure (10%), diphtheritic myocarditis with acute kidney injury (3.4%), fulminant hepatic failure (3.34%), severe thrombocytopenia

with intracranial hemorrhage (3.34%), respiratory distress (3.34%), and very severe pneumonia (6.66%). Incompatibility of blood is reportedly common in warm antibody AIHA, hence, extended red cell genotyping and studies of antibody specificity should be undertaken before the first transfusion. In cold antibody cases, the use of a bedside blood warmer is helpful. We experienced difficulties in arranging a cross-matched sample for nine children. A literature review reveals that the "best match" or "least incompatible units" can be transfused to such patients under close supervision without any serious side effects.[12] In an emergency, transfusions should not, however, be deferred due to the non-availability of the "least incompatible unit" as the risk of allergic transfusion reactions is low.[13]

Not much data are available regarding the role of IVIG in AIHA and Evans syndrome and can be added to treat children with severe illnesses with thrombocytopenia.[14,15] Cardiovascular complications of severe anemia and secondary causes contribute to the need for intensive care in children with AIHA. Early identification and emergency management with support from a well-equipped transfusion facility probably contributed to a good outcome in terms of mortality.

Conclusion

Identifying secondary causes of pediatric AIHA are essential and larger data from multiple centers will contribute toward creating the best clinical approach and emergency management of children with AIHA. Further studies are recommended in this direction for better understanding and implementation.

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